SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	INAVIR® DRY POWDER INHALER 20mg
Name of Active Ingredient	Laninamivir Octanoate Hydrate（JAN）
Title of Study	A Phase 4 Study of CS-8958 − A randomized double-blind controlled study of laninamivir comparing with oseltamivir for the treatment of influenza in patients with chronic respiratory diseases −
Investigators	
Study Centre(s)	
Publication (reference)	J Infect Chemother. (Accepted: 17 July 2012, Published online: 21 August 2012)
Studied Period	
Phase of Development	Phase IV
Objectives	The objective of this study is to evaluate the safety and efficacy of CS-8958 inhaled once comparing with oseltamivir in patients with type A or type B influenza virus infection complicated by chronic respiratory diseases.
Methodology	Multi-center, randomized, 2-parallel-group, double-blind, active-controlled study
Number of Patients (planned and analyzed)	Planned number of subjects: 200 subjects (100 subjects in the CS-8958 group, 100 subjects in the oseltamivir group) Full analysis set (FAS): 201 subjects (101 subjects in the CS-8958 group, 100 subjects in the oseltamivir group)
Diagnosis and Main Criteria for Inclusion	Patients with type A or B influenza virus infection who met all of the following inclusion criteria were eligible to participate in the study. 1) Patients diagnosed with influenza virus infection by the investigators 2) Body temperature (axillary) ≥ 37.5°C at the time of informed consent 3) Within 36 hours after the onset of any influenza symptoms (fever [feeling of fever], headache, myalgia/arthralgia, fatigue, chill/sweating, nasal symptoms, sore throat, cough) at

	the time of informed consent 4) Patients diagnosed with chronic respiratory diseases (e.g., bronchial asthma and chronic obstructive pulmonary disease). 5) Aged ≥ 20 years as of informed consent
Test Product, Dose and Mode of Administration	CS-8958 CS-8958 placebo Subjects inhaled a single dose of CS-8958 or CS-8958 placebo as a single inhalation on Day1.
Duration of Treatment	1) CS-8958 group: Single dose (5 days for the control drug) 2) Oseltamivir group: 5 days
Reference Therapy, Dose and Mode of Administration	Oseltamivir phosphate 75 mg capsule Oseltamivir phosphate placebo capsule Subjects in the oseltamivir phosphate group received 75 mg (as oseltamivir) orally twice daily for 5 days.
Criteria for Evaluation	Primary Endpoint: Time to Alleviation of Influenza Illness
Statistical Method	Efficacy Analysis; Primary analysis: The difference in the median time to alleviation of influenza illness between the CS-8958 group and the oseltamivir group (CS-8958 group − oseltamivir group) was calculated, and the 95% confidence interval (CI) was then calculated based on the generalized Wilcoxon test statistics. A generalized Wilcoxon test was performed with the oseltamivir group as the comparator. Safety Analysis; Adverse Events: The number of subjects with adverse events and the incidence of adverse events were presented by causal relationship (all/drug-related) for each treatment group. Serious adverse events, severe adverse events, and adverse events leading to discontinuation were summarized in the same manner. The number of subjects with individual adverse events and the incidence of individual adverse events were also presented by causal relationship (all/drug-related) as well as by severity and causal relationship (all/drug-related) for each treatment group.
Summary - Conclusion	The median time to illness alleviation was 64.7 h in the laninamivir group and 59.7 h in the oseltamivir group no significant difference was found between the treatment groups. The incidence of influenza-associated complications (pneumonia, bronchitis, otitis media, and sinusitis) was 5.9% (6/101) in the laninamivir group

	and 7.0% (7/100) in the oseltamivir group. The rate of exacerbation of the underlying disease was 7.9% (8/101) in the laninamivir group and 7.0% (7/100) in the oseltamivir group. Laninamivir octanoate showed similar efficacy and safety to oseltamivir in the treatment of influenza in patients with chronic respiratory diseases.
Date of Report	September 5, 2012